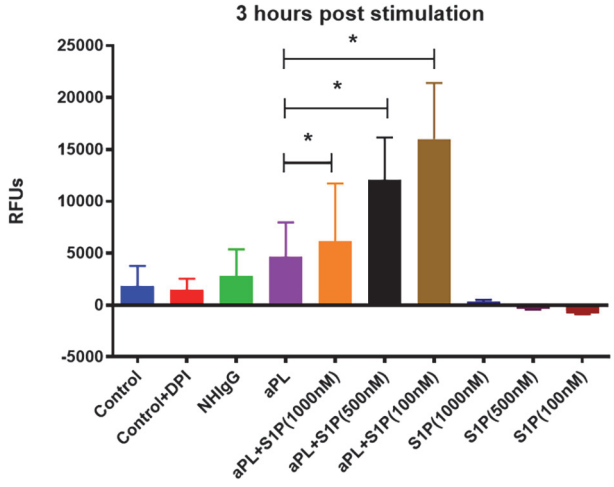
Conclusions This study comprehensively profiled the serum metabolites of primary APS patients and identified metabolic biomarkers that have the potential to be used as a diagnostic tool for differentiating APS from healthy controls. The APS metabolome analysis also revealed a potential significant role of S1P/S1PR axis in APS pathogenesis.



Abstract LSO-013 Figure 1

The effect of S1P on aPL mediated NETosis. aPL mediated NETosis was significantly potentiated by S1P in a concentration dependent manner. S1P did not trigger NETosis by itself.

Short oral presentation session 3: SLE biomarkers 1

LSO-014 CLINICO-PATHOLOGICAL ASSOCIATION OF SERUM CD44 LEVEL IN LUPUS NEPHRITIS PATIENTS

Susan Yung*, Lucy Gao, Tak Mao Chan. *Department of Medicine, School of Clinical Medicine, The University of Hong Kong, Hong Kong*

10.1136/lupus-2023-KCR.55

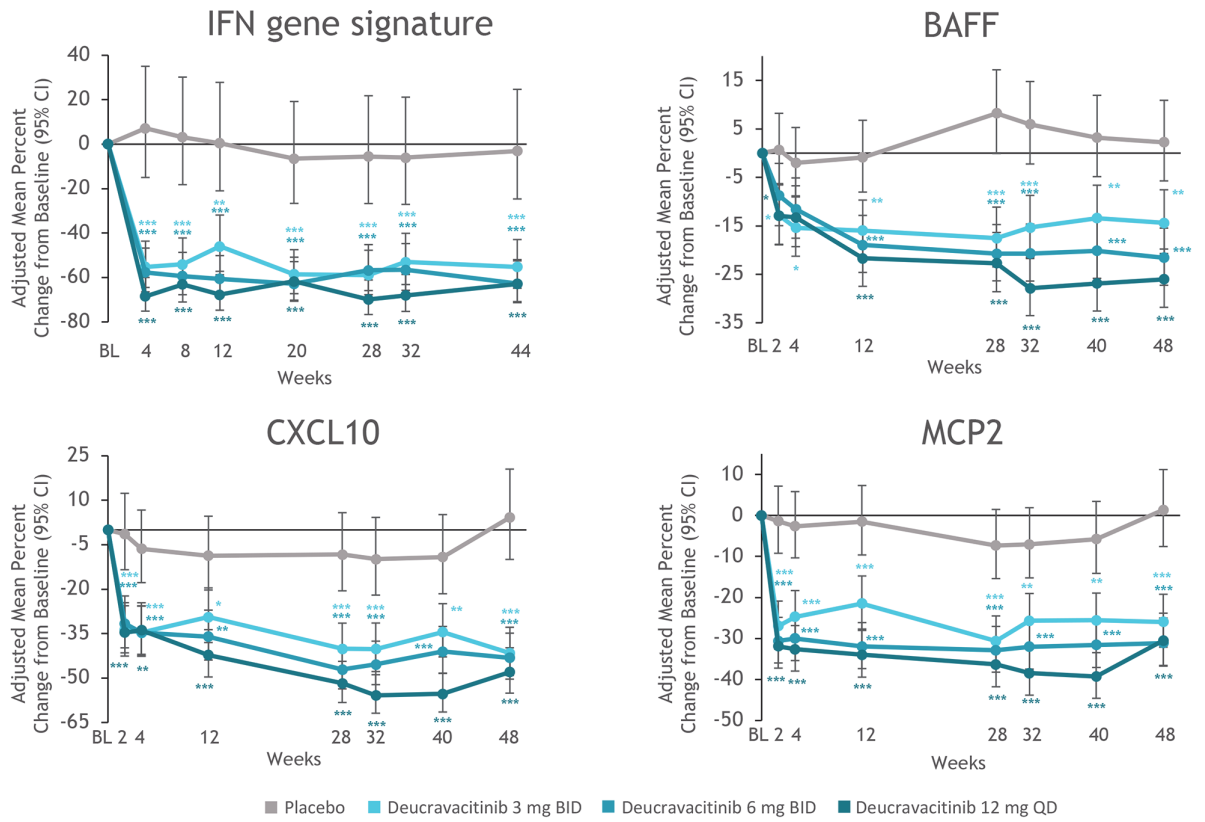
Background Conventional serological markers do not always correlate with clinical activity in lupus nephritis (LN). CD44 is a transmembrane glycoprotein that is widely expressed in immune and non-immune cells, and is implicated in tissue inflammation and fibrosis. CD44 also serves as a cell receptor for hyaluronan (HA), a glycosaminoglycan that contributes to inflammatory and fibrosis processes. This study investigated clinico-pathological associations of circulating CD44 level.
Methods Serial serum samples from patients with biopsy-proven Class III/IV LN were collected at intervals of 3–4 months over 3 to 4 years. Sera from sex- and age-matched patients with non-renal SLE or non-lupus chronic kidney disease (CKD) or healthy subjects served as Controls. Serum CD44 level was measured by ELISA
Results Six hundred and sixty-seven sera from 41 patients with LN (31 female and 10 male, age 38.78±12.02 years) were included. Serum CD44 level was significantly higher in active LN compared to remission, non-renal SLE, CKD, or healthy subjects (P<0.001, for all). Serum CD44 level correlated with SLEDAI-2K and renal SLEDAI-2K scores, anti-dsDNA antibody titre, proteinuria, and serum HA level, and inversely correlated with eGFR and C3 level (P<0.001, for all). Serum CD44 level increased at the time of nephritic flare and decreased after treatment with immunosuppression. A temporal relationship was observed between CD44 level and SLEDAI-2K or renal SLEDAI-2K scores, anti-dsDNA antibody and C3 levels, and proteinuria. ROC analysis showed that serum CD44 level distinguished active LN from healthy subjects (sensitivity 98.31%, specificity 100.00%), from quiescent LN (sensitivity 86.44%, specificity 98.31%), from non-renal SLE (sensitivity 98.31%, specificity 95.24%), and from non-lupus CKD (sensitivity 98.31%, specificity 100.00%) (P<0.0001, for all).
Conclusions Active LN is associated with increased serum CD44 level. Further studies are required to determine whether CD44 can serve as a clinically useful biomarker in the diagnosis and monitoring of LN activity.

LSO-015 DEUCRAVACITINIB REDUCES INTERFERONS, B CELL PATHWAYS, AND SEROLOGICAL BIOMARKERS OF SYSTEMIC LUPUS DISEASE ACTIVITY: PHARMACODYNAMIC ANALYSIS FROM THE PHASE 2 PAISLEY STUDY

[1]J Michelle Kahlenberg, [2]Ignacio Sanz, [3]Chun Wu, [3]Yanhua Hu, [4]Jin Hyang Kim, [5]Shalabh Singhal, [6]Ian M Catlett*. *[1]Rheumatology, University of Michigan, USA; [2]Rheumatology, Emory University, USA; [3]Informatics and Predictive Sciences, Bristol Myers Squibb, USA; [4]Translational Bioinformatics, Bristol Myers Squibb, USA; [5]Clinical Development, Bristol Myers Squibb, USA; [6]Translational Medicine, Bristol Myers Squibb, USA*

10.1136/lupus-2023-KCR.56

Background Tyrosine kinase 2 (TYK2) mediates signaling of key cytokines (eg, Type 1 IFNs, IL-23, and IL-12) involved in lupus pathogenesis. Deucravacitinib is a first-in-class, oral, selective, allosteric TYK2 inhibitor approved in multiple countries for the treatment of adults with plaque psoriasis.[1 2] Deucravacitinib was efficacious in a phase 2 trial in patients with active SLE (PAISLEY; NCT03252587).[3] This analysis evaluated the effect of deucravacitinib on biomarkers of TYK2-mediated pathways, B cell pathways, and serological biomarkers in patients in the phase 2 PAISLEY SLE trial.
Methods The 48-week PAISLEY trial randomized 363 patients with SLE 1:1:1:1 to placebo or deucravacitinib 3 mg twice daily (BID), 6 mg BID, or 12 mg once daily (QD). Whole blood transcripts, serum proteins, blood cell subsets, and antibody profiles were measured by immunoassays and flow cytometry.
Results With deucravacitinib treatment, significant reductions were observed in IFNα (at week 48) and IFNλ (week 2 through week 48), and IFNγ was numerically lower after week 12. Deucravacitinib, but not placebo, reduced IFN-regulated gene (IRG) expression as well as expression of cytokines and chemokines downstream of IFN activity, including BAFF, CXCL10, and MCP2 (figure 1). IFNλ, CXCL10, CCL19, and MCP2 were significantly reduced in the BID-dosed arms as early as 2 to 3 days after dose initiation. With deucravacitinib treatment, lymphocyte and neutrophil counts and complement levels increased, while markers associated with B cell activation and differentiation including BLC (CXCL13), CD38 (gene expression), and autoantibodies were reduced.
Conclusions Deucravacitinib suppressed IFN production, IRG expression, IFN-inducible proteins, B cell pathway markers,



*P<0.05; **P<0.01; ***P<0.001. Adjusted P values vs placebo. The mixed-effects model included fixed effects of treatment group, analysis visit, treatment-by-analysis visit interaction, and randomization stratum, and the continuous fixed covariate of baseline biomarker.
BAFF, B-cell activating factor; BID, twice daily; BL, baseline; CI, confidence interval; CXCL, chemokine ligand; IFN, interferon; MCP, monocyte chemoattractant protein; QD, once daily.

Abstract LSO-015 Figure 1 Deucravacitinib, but not placebo, reduced biomarkers of IFN activity and lupus pathophysiology

and serological biomarkers, consistent with clinical symptom improvements in SLE patients treated with deucravacitinib. Suppression of both IFN and B cell pathways suggests a broad reduction in lupus pathophysiology. These results provide a molecular framework for understanding how deucravacitinib modifies molecular networks in SLE.

REFERENCES

1. Armstrong A, *et al. J Am Acad Dermatol.* 2023;**88**(1):29–39.
2. Strober B, *et al. J Am Acad Dermatol.* 2023;**88**(1):40–51.
3. Morand E, *et al. Arthritis Rheumatol.* 2022 Nov 11 (Epub ahead of print).

LSO-016 ACTIVATED LEUKOCYTE CELL ADHESION MOLECULE, HEMOPEXIN, AND PEROXIREDOXIN 6 AS A POTENTIAL URINE BIOMARKER FOR KOREAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

[1]Ji-Won Kim*, [1,2]Chang-Hee Suh, [2]Wook-Young Baek, [2]Sang-Won Lee, [1]Ju-Yang Jung, [1]Hyoun-Ah Kim. *[1]Department of Rheumatology, Ajou University School of Medicine, Republic of Korea; [2]Department of Molecular Science and Technology, Ajou University School of Medicine, Republic of Korea*

10.1136/lupus-2023-KCR.57

Background This study aimed to demonstrate the potential of Activated Leukocyte Cell Adhesion Molecule (ALCAM), hemopexin, and peroxiredoxin (PRDX) 6 as urine biomarkers for systemic lupus erythematosus (SLE).

Methods We collected urine samples from 138 patients with SLE from Ajou Lupus Cohort and 39 healthy controls (HC). The concentrations of urine biomarker levels were analyzed by enzyme-linked immunosorbent assay kits specific for ALCAM, hemopexin and PRDX 6, respectively, according to the manufacturer's protocols. Receiver operating characteristic (ROC) curve analysis was performed to evaluate diagnostic utility and Pearson's correlation analysis was conducted to assess the relationships among the disease activity and urine biomarkers.

Results Patients with SLE showed a 5.7-fold increase in urinary ALCAM levels compared to HCs (6,760.5 pg/ml vs. 1,192.6 pg/ml, $p < 0.001$). In urinary hemopexin and PRDX6, the average levels were also significantly higher in patients with SLE compared to HCs (hemopexin, 649.8 ng/ml vs. 202 ng/ml, $p < 0.001$; PRDX6, 0.78 ng/ml vs. 0.17 ng/ml, $p = 0.003$). ALCAM, hemopexin, and PRDX6 showed more significant diagnostic value, especially for lupus nephritis (LN), and the area under the receiver operating characteristic curve for LN was 0.850 for ALCAM (95% CI, 0.778–0.921), 0.781 for hemopexin (95% CI, 0.695–0.867), and 0.714 for salivary S100A8 (95% CI, 0.617–0.812). In correlation analysis, all were significantly associated with anti-double stranded DNA (ALCAM, $r = 0.350$, $p < 0.001$; hemopexin, $r = 0.346$, $p < 0.001$; PRDX6, $r = 0.191$, $p = 0.026$) and SLEDAI (ALCAM, $r = 0.526$, $p < 0.001$; hemopexin, $r = 0.479$, $p < 0.001$; PRDX6, $r = 0.262$, $p = 0.002$).

Conclusions Urinary ALCAM, hemopexin and PRDX 6 were highly expressed patients with SLE compared to HCs. Thus, we suggest that urinary ALCAM, hemopexin and PRDX 6 can be potential biomarkers for SLE, especially valuable in the diagnosis of LN.